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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/637,550	08/11/2000	Chao-Feng Zheng	25436/1490	7640

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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS / STR
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/637,550	Zheng et al
Examiner	**Art Unit**
Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 16, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *10-23, 25, and 26* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-9 and 24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 17
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed January 16, 2003, Paper No. 16.

Claims 1-26 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

Response to Arguments and Amendments

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "said parent" lacks antecedent basis. Appropriate correction is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, and further in view of Lin et al, Weider et al and Gopal insofar as the claims are drawn to a cell line such as HeLa cells (or kit thereof) comprising a stably integrated recombinant nucleic acid construct comprising a reporter gene such as luciferase operably linked to the GAL4 recognition sequence for a sequence specific DNA binding protein, and which cell line further comprises a stably integrated recombinant nucleic acid construct encoding a constitutively expressed fusion protein comprising a conditionally active transactivation domain of CHOP downstream of and linked to the GAL4 DNA binding domain, wherein binding of said fusion protein to the GAL4 recognition sequence results in transactivation and increased expression of said reporter gene when said transactivation domain of CHOP, fused to the GAL4 DNA binding domain, is activated.

Wang et al teach transfected mammalian cells comprising a constitutively expressed fusion construct comprising the conditionally active transactivation domain of CHOP downstream of and linked to a GAL4 DNA binding domain, and which transfected cells further comprise a reporter plasmid comprising a luciferase reporter gene operably linked to the GAL4 recognition sequence, whereby the transactivation of CHOP, following GAL4 binding to the recognition sequence, leads

to increased expression of the reporter gene (luciferase) over basal or constitutive levels of expression in the mammalian host cell (See entire document, especially figure 3 and last two paragraphs of the text (pages 1348-1349).

Wang et al does not teach the stable transfection of HeLa cells with the claimed nucleic acid constructs.

Lin et al teach the participation and interactions of various kinase cascades in cellular growth and differentiation, including the participation of stress activated protein kinases such as p38, which is a known activator of CHOP, in various cell lines including HeLa cells (See the abstract and first paragraph of the introduction on page 286; figures 4 and 6 on pages 288 and 289, respectively; and the last paragraph of the document on page 290).

Wieder et al teach the stable transfection of fibroblast derived cells including HeLa cells with various nucleic acid constructs (See col. 4, lines 11-16; col. 7, lines 20-32; col. 11).

Gopal teaches the stable and transient transfection of various mammalian cell lines (See entire document, especially Table 2 on page 1189).

It would have been obvious to one of ordinary skill in the art to transfect mammalian cells with a recombinant nucleic acid construct comprising a reporter gene operably linked to the GAL4 recognition sequence, and additionally with a nucleic acid construct encoding a fusion protein comprising the transactivation domain of CHOP operably linked to the GAL4 binding domain because these constructs had been transfected into the fibroblast derived mouse cell line NIH3T3 cell line, as taught previously by Wang et al. One of ordinary skill in the art would have

been motivated to study the regulation of CHOP in appropriate host cell lines (or using a kit comprising an appropriate host cell line) because CHOP has been implicated as being involved in kinase cascades which affect cellular events such as growth, differentiation and apoptosis, as taught previously by Wang et al and Lin et al. One of ordinary skill in the art would have expected that various mammalian cell lines are optionally stably or transently transfected, depending on the method of transfection utilized, because the option of stably or transiently transfecting appropriate cells had been known and performed routinely in the art, as described in 1985 by Gopal. One of ordinary skill in the art would have been motivated to stably transfect the nucleic acid constructs (described above) into fibroblast derived cell lines such as NIH3T3 and HeLa cells in order to study the role of CHOP activation on cellular functions and activities because these fibroblast derived cell lines have been found to contain stress activated protein kinases, such as p38, known to activate the transcription factor CHOP, as taught previously by Wang et al and Lin et al, and one would have been motivated to study various forms of regulation of (the transactivation of) CHOP in appropriate stably transformed host cell lines known to participate in stress activation and other forms of regulation of kinase cascades involving CHOP. In addition, one of ordinary skill in the art would have been motivated to produce stable transfectants in these appropriate host cell lines rather than transient transfectants because stable transfectants provide a relatively permanent source of transfectants which express a reproducible amount of transfected nucleic acid constructs when the transfected cell line is grown under reproducible conditions, as opposed to transient transfectants, which cells are short-lived, and

which must be generated anew with each experiment, and which provide variable levels of nucleic acid expression with every transfection. One of ordinary skill in the art would have expected that HeLa cells are appropriate host cells for stable transfections because stably transfecting HeLa cells is a routine technique known in the art as described by Wieder et al, who teach the stable transfection of HeLa cells using appropriate compatible nucleic acid constructs required for stable expression in the HeLa cell environment. One of ordinary skill in the art would have been motivated to study the regulation of CHOP activation in HeLa cells because Lin et al teach the use of HeLa cells to study the interaction and participation of various kinase cascades in stress activation, including the participation and activation of p38, a known activator of CHOP. One of ordinary skill in the art therefore would have expected that the stably transfected HeLa cells provide an appropriate reagent to study the regulation of CHOP activation, including stress activation.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM R. SHUKLA, PH.D
PATENT EXAMINER

JZ

April 6, 2003